Approved for use through 10/31/2002. OMB 0651-0031 e type a plus sign (+) inside this box --> 🛨 U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE der the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number. **Application Number** 10/005.344 TRANSMITTAL Filing Date December 4, 2001 **FORM First Named Inventor** Loren J. Miraglia (to be used for all correspondence after initial filing) Group Art Unit 1635 T. Gibbs **Examiner Name** otal Number of Pages in This Submission Attorney Docket Number ISIS0052-100/ISPH-0622 ENCLOSURES (check all that apply) Assignment Papers After Allowance Communication to Fee Transmittal Form (for an Application) Group Appeal Communication to Board of Fee Attached ☐ Drawing(s) Appeals and Interferences Amendment / Response Licensing-related Papers (Appeal Notice, Brief, Reply Brief) After Final Petition Proprietary Information Petition to Convert to a Status Letter ☐ Affidavits/declaration(s) Provisional Application Power of Attorney with Revocation Other Enclosure(s) Extension of Time Request and Change of Correspondence (please identify below): Address Table A Terminal Disclaimer Express Abandonment Request Statement Under 37 CFR 3.73(b) Request for Refund with executed Assignment ☐ Information Disclosure Statement CD, Number of CD(s) Certified Copy of Priority Remarks Document(s) Response to Missing Parts/ Incomplete Application Response to Missing Parts under 37 CFR 1.52 or 1.53 SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231 on this date:

Typed or printed name

Paul K. Legaard, Registration No. 38,534

Signature

Date

12 January 2004

Paul K. Legaard, Registration No. 38,534

Firm

Individual name

Signature

Burden Hour Statement: This form is estimated to take 0.2 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be send to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.



## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Assistant Commissioner for Patents Washington, DC 20231

Sir:

# POWER OF ATTORNEY WITH REVOCATION AND CHANGE OF CORRESPONDENCE ADDRESS

I hereby revoke all previous powers of attorney or authorizations of agent given in the patents/applications identified in Table A attached hereto, and appoint

▼ Practitioners at Customer Number: 34138 as my/our attorney(s) or agent(s) to prosecute the patents/applications identified in Table A, and to transact all business in the United States Patent and Trademark Office connected therewith. Please change the Correspondence Address for the patent applications identified in Table A to: ▼ Practitioners at Customer Number: 34138 I am the: ☐ Applicant/Inventor. Assignee of record of the entire interest. (A statement under 37 CFR 3.73(b) is enclosed.) Respectfully submitted, ISIS PHARMACEUTICALS, INC. Mame: B. Lynne Parshall Title: Executive Vice President



## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Assistant Commissioner for Patents Washington, DC 20231

Sir:

### STATEMENT UNDER 37 CFR 3.73(b)

Applicant, ISIS Pharmaceuticals, Inc., a corporation, states that it is:

the assignee of the entire right, title, and interest of the patent applications identified in Table A attached hereto.

The extent (by, percentage) of its ownership interest is 100% in the patent applications identified in Table A.

By:

a copy of the pertinent assignment from the inventor(s) of the patent applications identified in Table A is enclosed herewith.

The undersigned (whose title is supplied below) is authorized to act on behalf of the assignee.

Respectfully submitted,

ISIS PHARMACEUTICAES, INC.

Date: 11-6-03

Name: B. Lynne Parshall

Title: Executive Vice President

DOCKET NO.: ISPH-0622 PATENT

#### ASSIGNMENT

WHEREAS, We, Loren J. Miraglia of Encinitas, State of California, Pamela Nero of San Diego, State of California, Mark J. Graham of San Clemente, State of California, Brett P. Monia of Encinitas, State of California, Erich Koller of Carlsbad, State of California, Ming Yi Chang of San Diego, State of California and Mane Manoharan of Carlsbad, State of California; have invented a certain invention entitled Antisense Modulation of Human MDM2 Expression, for which we have made application for Letters Patent of the United States, said application having been filed December 4, 2001 and assigned Application No. 10/005,344; and

WHEREAS, ISIS Pharmaceuticals, Inc. hereinafter referred to as the assignee, of 2292 Faraday Avenue, Carlsbad CA, a corporation of Delaware, is desirous of acquiring the entire right, title and interest in and to the said inventions or improvements and in and to the said application, and in, to and under any and all Letters Patent which may be granted on or as a result thereof in any and all countries:

NOW, THEREFORE, for and in consideration of the sum of One Dollar (\$1.00) to each of us in hand paid by said assignee, and other good and valuable consideration, the receipt of which is hereby acknowledged, we, the said assignors, have sold, assigned, transferred and set over, and by these presents do hereby sell, assign, transfer and set over to said assignee, the entire right, title and interest in and to said inventions or improvements and said application and any and all continuations, divisions and renewals of and substitutes for said application, and in, to and under any and all Letters Patent which may be granted on or as a

DOCKET NO.: ISPH-0622 PATENT

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result thereof in the United States and any and all other countries, and any reissue or reissues or extension or extensions of said Letters Patent, and assign to and authorize said assignee, to file in our names applications for Letters Patent in all countries, the same to be held and enjoyed by said assignee, its successors, assigns, nominees or legal representatives, to the full end of the term or terms for which said Letters Patent respectively may be granted, reissued or extended, as fully and entirely as the same would have been held and enjoyed by us had this assignment, sale and transfer not been made.

AND we hereby covenant that we have full right to convey the entire interest herein assigned, and that we have not executed and will not execute any agreement in conflict herewith, and we further covenant and agree that we will each time request is made and without undue delay, execute and deliver all such papers as may be necessary or desirable to perfect the title to said inventions or improvements, said application and said Letters Patent to said successors, assigns, nominees, or legal assignee, its representatives, and each of us agrees to communicate to said assignee or to its nominee all known facts respecting said inventions or improvements, said application and said Letters Patent, to testify in any legal proceedings, to sign all lawful papers to execute all disclaimers and divisional, continuing, reissue and foreign applications, to make all rightful oaths, and generally to do everything possible to aid said assignee, successors, assigns, nominees and legal representatives to obtain and enforce for its or their own benefit proper patent protection for said inventions or improvements in any and all countries.

DOCKET NO.: ISPH-0622

PATENT

AND we hereby authorize and request the Commissioner of Patents and Trademarks of the United States and any official of any country or countries foreign to the United States whose duty it is to issue patents on applications as aforesaid, to issue to said assignee, as assignee of the entire right, title and interest, any and all Letters Patent for said inventions or improvements, including any and all Letters Patent of the United States which may be issued and granted on or as a result of the application aforesaid, in accordance with the terms of this assignment.

IN WITNESS WHEREOF, we have hereunto set our hands and seals.

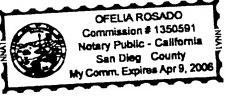
DATED: My 20 , 2002

Jour Miraghe Loren D. Miraghia

On this 20 day of Moy, 2002, before me, the undersigned, a Notary Public for the state, personally appeared Loren J. Miraglia, personally known to me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that he/she executed the same in his/her authorized capacity, and that by his/her signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.

WITNESS my hand and official seal.

Oflin Mosodo
Signature of Notary



•	DOCKET NO.: ISPH-0622		PATENT
	DATED:, 2002	Pamela Nero	
•	State of California County of San Diego	) ) ss. )	
	Pamela Nero, personall satisfactory evidence to Assignment and acknowled authorized capacity, a	day of, 2002 Public for the state, person who subscripted to me that she execute and that by her signature of tity on behalf of which to.	on the basis of bed the foregoing d the same in her on the Assignment
		WITNESS my hand and offic	cial seal.
		Signature of Notary	<u> </u>
	DATED: April 19, 2002	Mark J. Graham	
	Mark J. Graham, person of satisfactory evider foregoing Assignment a same in his authorized	day of, 200 Public for the state, personally known to me/proved to acce to be the person who su and acknowledged to me that d capacity, and that by his or the entity on behalf o	<pre>me on the basis bscribed the  he executed the  signature on the</pre>
The Salvation of the	LANE B.D. SCHWARTZ Commission # 1196197 Notary Public - Callication San Diego County My Comm. Expires Sep 13, 2002	WITNESS my hand and offi	cial seal.

DOCKET NO.: ISPH-0622	PATENT
DATED: 5/9, 2002	Brett P. Monia
State of California County of San Diego	) ) ss. )
Brett P. Monia, persona of satisfactory evidence foregoing Assignment as same in his authorized	day of May 2002, before me, the Public for the state, personally appeared ally known to me/proved to me on the basis be to be the person who subscribed the adacknowledged to me that he executed the capacity, and that by his signature on the or the entity on behalf of which the the Assignment.
PAMELA GROOMS Commission # 1296342 Notary Public - California San Diego County My Comm. Expires Mar 8, 2005	WITNESS my hand and official seal.  Signature of Notary
DATED: <u>4/22/02</u> , 2002	Frich Koller

On this day of first, 2002, before me, the undersigned, a Notary Public for the state, personally appeared Erich Koller, personally known to me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that he executed the same in his authorized capacity, and that by his signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.

ss.

LANE B.D. SCHWARTZ
Commission # 1196197
Notary Public - California
San Diego County
My Comm. Boires Sep 13, 2002

State of California

County of San Diego

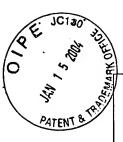
WITNESS my hand and official seal.

DOCKET NO.: ISPH-0622	PATENT
DATED: <u>5 - /</u> , 2002	Aing Yi Chifang
State of California County of San Diego	) ) ss. )
undersigned, a Notary I Ming Yi Chiang, persons of satisfactory evident foregoing Assignment at the same in his/her aut signature on the Assign of which the person act laneables CHWARTZ	Signature of Notary  Muhah Meshin
State of California County of San Diego	Mano Manoharan  MUTHIAH  ss.
undersigned, a Notary  Mano Manoharan, person of satisfactory eviden foregoing Assignment a same in his authorized	day of, 2002, before me, the Public for the state, personally appeared ally known to me/proved to me on the basis ce to be the person who subscribed the nd acknowledged to me that he executed the capacity, and that by his signature on the or the entity on behalf of which the the Assignment.
LANE B.D. SCHWARTZ  - Commission # 1196197  Notary Public - California San Diego County My Comm. Expires Sep 13, 2002	WITNESS my hand and official seal.  Signature of Notary



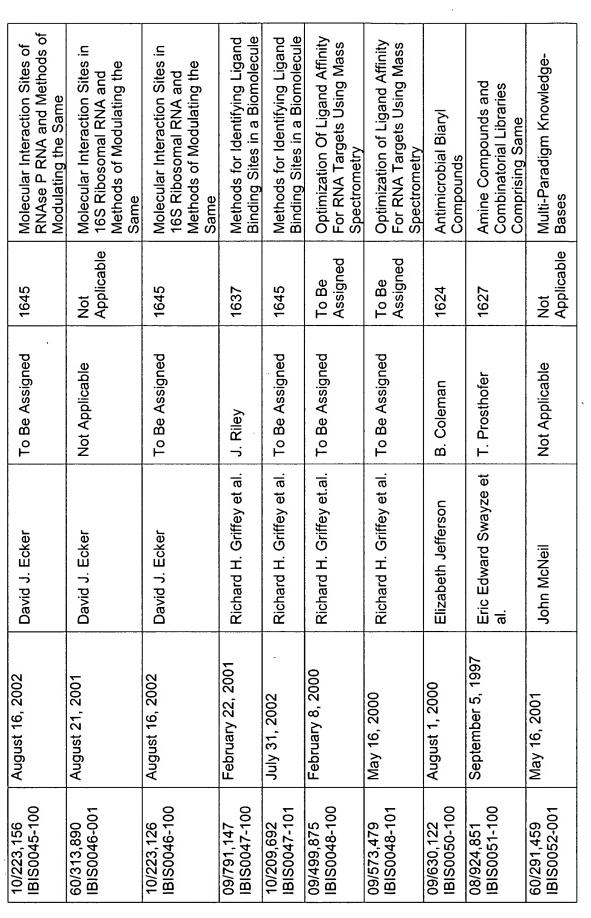
Table A

					MARK
Serial No. Patent No. Docket No.	Filing Date Issue Date	Inventor(s)	Examiner	Art Unit	Title
09/200,355 6,451,524 IBIS0010-100	November 25, 1998 September 17, 2002	David J. Ecker	J. Fredman	1655	Identification of Disease Predictive Nucleic Acids
09/200,107 6,492,111 IBIS0034-100	November 25, 1998 December 10, 1998	David J. Ecker	J. Fredman	1634	IN SITU Binary Synthesis of Biologic00ally Effective Molecules
10/209,761 IBIS0034-101	August 1, 2003	David J. Ecker	To Be Assigned	1634	IN SITU Binary Synthesis of Biologically Effective Molecules
09/076,440 6,221,587 IBIS0035-100	May 12, 1998 April 24, 2001	David J. Ecker et al.	E. Campbell	1656	Identification of Molecular Interaction Sites in RNA for Novel Drug Discovery
09/310,667 IBIS0035-101	May 12, 1999	David J. Ecker et al.	F. Lu	1634	Identification of Molecular Interaction Sites in RNA for Novel Drug Discovery
09/076,405 IBIS0036-100	May 12, 1998	Richard Griffey et al.	S. Broda	2123	Generation of Virtual Combinatorial Libraries of Compounds
09/753,869 IBIS0036-101	January 3, 2001	Richard Griffey et al.	M. Borin	1631	Generation of Virtual Combinatorial Libraries of Compounds
09/076,447 IBIS0037-100	May 12, 1998	Richard Griffey et al.	J. Fredman	1655	Characterization of Interactions Between Molecular Interaction Sites of RNA and Ligands Therefor



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09/310,653 IBIS0037-101	May 12, 1999	Richard Griffey et al.	J. Fredman	1637	Characterization of Interactions Between Molecular Interaction Sites of RNA and Ligands Therefor
09/076,206 6,428,956 IBIS0038-100	May 12, 1998 August 6, 2001	Stanley T. Crooke et al.	S. Zitomer	1634	Mass Spectrometric Methods for Biomolecular Screening
09/260,310 6,329,146 IBIS0038-101	March 2, 1999 December 11, 2001	Stanley T. Crooke	S. Zitomer	1634	Mass Spectrometric Methods for Biomolecular Screening
09/884,317 IBIS0038-102	June 19, 2001	Stanley T. Crooke	A. Chakrabarti	1634	Mass Spectrometric Methods for Biomolecular Screening
09/884,317 IBIS0038-103	June 27, 2003	Stanley T. Crooke	To Be Determined		Mass Spectrometric Methods for Biomolecular Screening
09/076,214 IBIS0039-100	May 12, 1998	Richard H. Griffey et al.	T. Friend	1639	Generation of Combinatorial Libraries of Compounds Corresponding to Virtual Libraries of Compounds
09/400,150 IBIS0039-101	September 21, 1999	Richard H. Griffey et al.	M. Tran	1639	Generation of Combinatorial Libraries of Compounds Corresponding to Virtual Libraries of Compounds
60/085,092 IBIS0040-001	May 12, 1998	Stanley T. Crooke	Not applicable	Not applicable	Small Molecule Targeting Of RNA Structures
09/076,404 IBIS0040-100	May 12, 1998	David J. Ecker et al.	A. Marschel	1631	Identification of Molecular Interaction Sites in RNA for Novel Drug Discovery
09/310,735 IBIS0040-101	May 12, 1999	David J. Ecker et al.	A. Marschel	1631	Modulation of Molecular Interaction Sites on RNA and Other Biomolecules

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10/104,949 IBIS0040-102	March 22, 2002	David J. Ecker et al.	A. Marschel	1631	Modulation of Molecular Interaction Sites on RNA and Other Biomolecules	
09/310,907 IBIS0041-100	May 12, 1999	David J. Ecker et al.	A. Marschel	1631	Molecular Interaction Sites of Vimentin RNA and Methods of Modulating the Same	
10/135,017 IBIS0041-101	April 24, 2002	David J. Ecker et al.	A. Marschel	1631	Molecular Interaction Sites of Vimentin RNA and Methods of Modulating the Same	
09/310,761 IBIS0042-100	May 12, 1999	David J. Ecker et al.	M. Schmidt	1635	Molecular Interaction Sites of Ornithine Decarboxylase RNA and Methods of Modulating the Same	
60/314,236 IBIS0043-001	August 22, 2001	David J. Ecker	Not Applicable	Not Applicable	Molecular Interaction Sites of Hepatitis C Virus RNA and Methods of Modulating the Same	
10/225,501 IBIS0043-100	August 19, 2002	David J. Ecker	To Be Assigned	1645	Methods for Identifying Ligand Binding Sites in a Biomolecule	
60/314,251 IBIS0044-001	August 22, 2001	David J. Ecker	Not Applicable	Not Applicable	Molecular Interaction Sites of 23S Ribosomal RNA and Methods of Modulating the Same	
10/224,836 IBIS0044-100	August 20, 2002	David J. Ecker	To Be Assigned	1645	Molecular Interaction Sites in 23S Ribosomal RNA and Methods of Modulating the Same	
60/314,020 IBIS0045-001	August 21, 2001	David J. Ecker	Not Applicable	Not Applicable	Molecular Interaction Sites of RNAse P RNA and Methods of Modulating the Same	





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10/150,668	May 16, 2002	John McNeil et al.	To Be Assigned	2176	Multi-Paradigm Knowledge-
IBIS0052-100					Bases
09/411,748	October 1, 1999	John McNeil	Patricia A. Bex	1743	System and Method for
6,429,016	August 6, 2002				Sample Positioning in a
IBIS0053-100					
10/153,327	May 22, 2002	John McNeil	To Be Assigned	1743	System and Method for
IBIS0053-101					Sample Positioning in a Robotic System
10/067,017	February 24, 2002	Michael L. Migawa	T. McKenzie	1624	Novel Pyranosyl Cytosines:
IBIS0054-100					Pharmaceutical Formulation and Methods
10/071,978 IBIS0055-100	February 6, 2002	Eric E. Swayze et al.	K. Habte	1624	Novel Benzimidazole
09/678.434			(		
IBIS0056-100	October 2, 2000		E. Quan	1/43	Self-Dispensing Storage Device
09/310,844 IBIS0058-100	May 12, 1999	David J. Ecker et al.	M. Schmidt	1635	Molecular Interaction Sites of
)					Interleukin-2 RNA and Methods of Modulating the
					Same
09/499,875 IBIS0059-100	February 8, 2000	Richard Griffey et al.	M. Tran	1639	Optimization of Ligand Affinity for RNA Targets Using Mass
7100					Spectrometry
U9/5/3,4/9 IBIS0059-101	May 16, 2000	Richard Griffey et al.	T. Prosthofer	1627	Optimization of Ligand Affinity for RNA Targets Using Mass
					Spectrometry
10/005,344 ISIS0052-100	December 4, 2001	Loren J. Miraglia et al.	T. Gibbs	1635	Antisense Modulation of Human MDM2 Expression

10/281,349 ISIS0002-105	October 25, 2002	Stanley T. Crooke	To Be Assigned	1635	Oligoribonucleotides and Ribonucleases for Cleaving RNA
10/327,805 ISIS0060-101	December 20, 2002	Brett P. Monia et al.	To Be Assigned	1635	Antisense Modulation of SMAD6 Expression

